AMENDMENTS TO THE CLAIMS:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims

1-13. (cancelled)

14. (currently amended) A cholesterol-lowering therapy method, which method comprises the administration of melagatran ~~a low molecular weight thrombin inhibitor,~~ or a pharmaceutically acceptable derivative thereof[[,]] to a patient in need of such therapy.

15. (cancelled)

16. (currently amended) The method ~~as claimed in~~ of Claim 14 ~~or Claim 15~~ wherein the therapy/treatment results in a decrease in serum levels of cholesterol, low-density lipoproteins, very low-density lipoproteins, triglycerides and/or apolipoprotein B; and/or an increase in serum levels of high-density lipoproteins and/or apolipoprotein A-I.

17. (cancelled)

18. (currently amended) The method ~~as claimed in~~ of Claim 14~~17~~, wherein the method comprises administering ~~derivative of melagatran is~~ a prodrug of melagatran.

19. (currently amended) The method ~~as claimed in~~ of Claim 18, wherein the method comprises delivering a prodrug ~~is~~ of the formula:

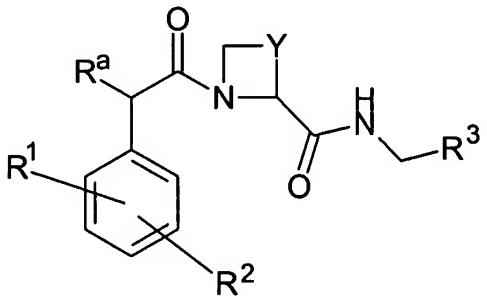
$$R^1O_2C\text{-}CH_2\text{-}(R)Cgl\text{-}(S)Aze\text{-}Pab\text{-}OH,$$

wherein R^1 represents linear or branched $C_{1\text{-}6}$ alkyl and the OH group replaces one of the amidino hydrogens in Pab.

20. (currently amended) The method ~~as claimed in~~ of Claim 19, wherein R^1 represents methyl, ethyl, or propyl.

21. (currently amended) The method ~~as claimed in~~ of Claim 20, wherein R^1 represents ethyl.

22. (currently amended) A cholesterol-lowering therapy method, which method comprises the administration of a thrombin inhibitor ~~The method as claimed in any one of Claims 14 to 16, wherein the thrombin inhibitor is~~ of formula I,



I

wherein

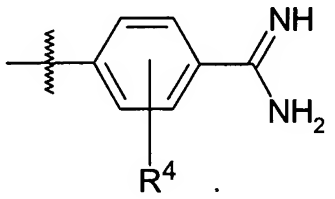
R^a represents -OH or $-CH_2OH$;

R^1 represents at least one optional halo substituent;

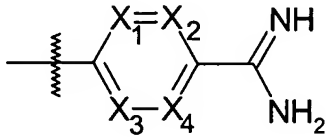
R^2 represents one or two C_{1-3} alkoxy substituents, the alkyl parts of which substituents are themselves substituted with one or more fluoro substituents;

Y represents $-CH_2-$ or $-(CH_2)_2-$; and

R^3 represents a structural fragment of formula I(i) or I(ii):



I(i)



I(ii)

wherein

R^4 represents H or one or more fluoro substituents; and

one or two of X_1, X_2, X_3, and X_4 represent -N- and the others represent -CH-,

or a pharmaceutically acceptable derivative thereof, to a patient in need of such therapy.

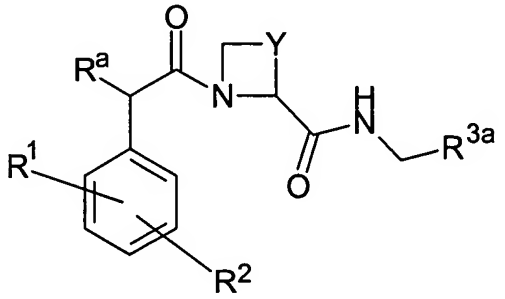
23. (currently amended) The method ~~as claimed in~~ of Claim 22, wherein the thrombin inhibitor or derivative is:

Ph(3-Cl)(5-$OCHF_2$)-(*R*)CH(OH)C(O)-(*S*)Aze-Pab;

Ph(3-Cl)(5-$OCHF_2$)-(*R*)CH(OH)C(O)-(*S*)Aze-Pab(2,6-diF); or
Ph(3-Cl)(5-OCH_2CH_2F)-(*R*)CH(OH)C(O)-(*S*)Aze-Pab.

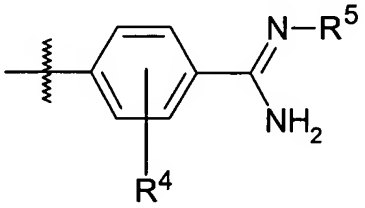
24. (currently amended) The method ~~as claimed in~~ of Claim 22 ~~or Claim 23~~, wherein the ~~derivative of~~ the thrombin inhibitor or derivative is a prodrug of a thrombin ~~that~~ inhibitor.

25. (currently amended) The method ~~as claimed in~~ of Claim 24, wherein the prodrug is of formula Ia,

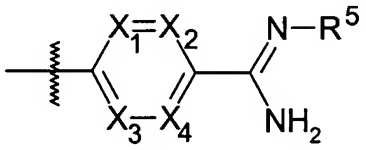


Ia

wherein R^{3a} represents a structural fragment of formula I(iii) or I(iv):



I(iii)



I(iv)

wherein R^5 represents OR^6 or $C(O)OR^7$;

R^6 represents H, C_{1-10} alkyl, C_{1-3} alkylaryl, or C_{1-3} alkyloxyaryl, [[(]]the alkyl parts of which latter two groups are optionally interrupted by one or more oxygen atoms, and the aryl parts of which latter two groups are optionally substituted by one or more substituents selected from halo, phenyl, methyl or methoxy, which latter three groups are also optionally substituted by one or more halo substituents[[)]]; and

R^7 represents C_{1-10} alkyl, ~~(which latter group is~~ optionally interrupted by one or more oxygen atoms;~~), or~~ C_{1-3} alkylaryl; or C_{1-3} alkyloxyaryl, [[(]]the alkyl parts of which latter two groups are optionally interrupted by one or more oxygen atoms, and the aryl parts of which latter two groups are optionally substituted by one or more substituents selected

from halo, phenyl, methyl or methoxy, which latter three groups are also optionally substituted by one or more halo substituents[[];]] ~~and~~

~~R^a, R^1, R^2, Y, R^4, X_1, X_2, X_3 and X_4 are as defined in Claim 22~~.

26. (currently amended) The method ~~as claimed in~~ of Claim 25, wherein the prodrug is:

Ph(3-Cl)(5-$OCHF_2$)-(*R*)CH(OH)C(O)-(*S*)Aze-Pab(OMe);

Ph(3-Cl)(5-$OCHF_2$)-(*R*)CH(OH)C(O)-(*S*)Aze-Pab(2,6-diF)(OMe); or

Ph(3-Cl)(5-OCH_2CH_2F)-(*R*)CH(OH)C(O)-(*S*)Aze-Pab(OMe).

27. (original) A combination product comprising:

(A) a low molecular weight thrombin inhibitor, or a pharmaceutically-acceptable derivative thereof; and

(B) another cholesterol-lowering, or lipid-lowering/modifying, therapeutic agent,

wherein each of components (A) and (B) is formulated in admixture with a pharmaceutically-acceptable adjuvant, diluent or carrier.

28-29. (cancelled)

30. (currently amended) ~~A~~ The combination product ~~as claimed in any one~~ of ~~Claims~~ Claim 27 ~~to 29~~, wherein the thrombin inhibitor or derivative is melagatran.

31. (currently amended) ~~A~~ The combination product ~~as claimed in~~ of Claim 27 ~~30~~, wherein the thrombin inhibitor or derivative ~~of melagatran~~ is a prodrug of melagatran.

32. (currently amended) ~~A~~ The combination product ~~as claimed in~~ of Claim 31, wherein the prodrug is of the formula:

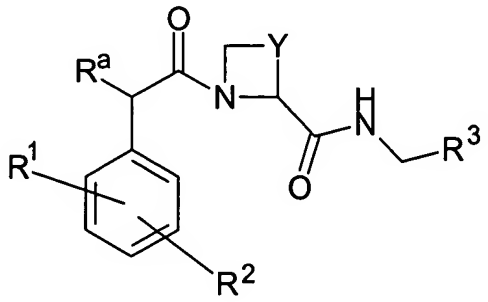
R^1O_2C-CH_2-(*R*)Cgl-(*S*)Aze-Pab-OH,

wherein R^1 represents linear or branched C_{1-6} alkyl and the OH group replaces one of the amidino hydrogens in Pab.

33. (currently amended) ~~A~~ The combination product ~~as claimed in~~ of Claim 32, wherein R^1 represents methyl, ethyl, or propyl.

34. (currently amended) ~~A~~ The combination product ~~as claimed in~~ of Claim 33, wherein R^1 represents ethyl.

35. (currently amended) ~~A~~ The combination product ~~as claimed in any one~~ of ~~Claims~~ Claim 27 ~~to 29~~, wherein the thrombin inhibitor or derivative is a compound of formula I,



I

wherein

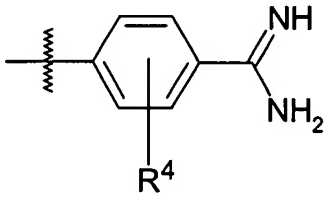
R^a represents -OH or $-CH_2OH$;

R^1 represents at least one optional halo substituent;

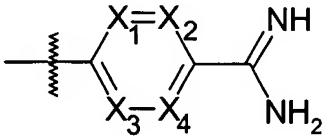
R^2 represents one or two C_{1-3} alkoxy substituents, the alkyl parts of which substituents are themselves substituted with one or more fluoro substituents;

Y represents $-CH_2-$ or $-(CH_2)_2-$; and

R^3 represents a structural fragment of formula I(i) or I(ii):



I(i)



I(ii)

wherein

R^4 represents H or one or more fluoro substituents; and

one or two of X_1, X_2, X_3, and X_4 represent -N- and the others represent -CH-.

36. (currently amended) ~~A~~ The combination product ~~as claimed in~~ of Claim 27 ~~Claim 35~~, wherein the thrombin inhibitor or derivative is:

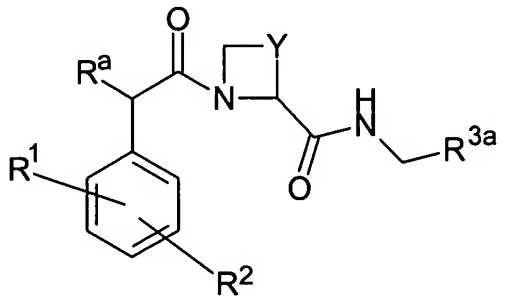
Ph(3-Cl)(5-$OCHF_2$)-(*R*)CH(OH)C(O)-(*S*)Aze-Pab;

Ph(3-Cl)(5-$OCHF_2$)-(*R*)CH(OH)C(O)-(*S*)Aze-Pab(2,6-diF); or

Ph(3-Cl)(5-OCH_2CH_2F)-(*R*)CH(OH)C(O)-(*S*)Aze-Pab.

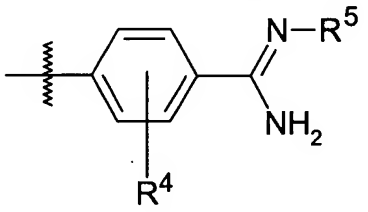
37. (currently amended) ~~A~~ The combination product ~~as claimed in~~ of Claim 27 ~~Claim 35 or Claim 36~~, wherein the thrombin inhibitor or derivative ~~of the thrombin inhibitor~~ is a prodrug of a thrombin ~~that~~ inhibitor.

38. (currently amended) ~~A~~ The combination product ~~as claimed in~~ of Claim 27 ~~Claim 37~~, wherein the thrombin inhibitor or derivative is a prodrug is of formula Ia,

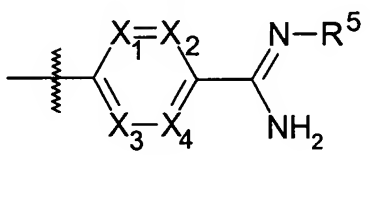


Ia

wherein R^{3a} represents a structural fragment of formula I(iii) or I(iv):



I(iii)



I(iv)

wherein R^5 represents OR^6 or $C(O)OR^7$;

R^6 represents H, C_{1-10} alkyl, C_{1-3} alkylaryl or C_{1-3} alkyloxyaryl, [[(]]the alkyl parts of which latter two groups are optionally interrupted by one or more oxygen atoms, and the aryl parts of which latter two groups are optionally substituted by one or more substituents selected from halo, phenyl, methyl or methoxy, which latter three groups are also optionally substituted by one or more halo substituents[[)]]; and

R^7 represents C_{1-10} alkyl, [[(]]which latter group is optionally interrupted by one or more oxygen atoms;~~), or~~ C_{1-3} alkylaryl; or C_{1-3} alkyloxyaryl, [[(]]the alkyl parts of which latter two groups are optionally interrupted by one or more oxygen atoms, and the aryl parts of which latter two groups are optionally substituted by one or more substituents selected

from halo, phenyl, methyl or methoxy, which latter three groups are also optionally substituted by one or more halo substituents~~); and~~

~~R^a, R^1, R^2, Y, R^4, X_1, X_2, X_3 and X_4 are as defined in Claim 35~~.

39. (currently amended) ~~A~~ The combination product ~~as claimed in~~ of Claim 27 ~~38~~, wherein the thrombin inhibitor or derivative ~~prodrug~~ is:

Ph(3-Cl)(5-$OCHF_2$)-(*R*)CH(OH)C(O)-(*S*)Aze-Pab(OMe);

Ph(3-Cl)(5-$OCHF_2$)-(*R*)CH(OH)C(O)-(*S*)Aze-Pab(2,6-diF)(OMe); or

Ph(3-Cl)(5-OCH_2CH_2F)-(*R*)CH(OH)C(O)-(*S*)Aze-Pab(OMe).

40. (currently amended) ~~A~~ The combination product ~~as claimed in any one~~ of ~~Claims~~ Claim 27 ~~to 39~~, wherein the other therapeutic agent is a statin.

41. (currently amended) ~~A~~ The combination product ~~as claimed in~~ of Claim 27, ~~40~~ wherein the other therapeutic agent ~~statin~~ is lovastatin, pravastatin, fluvastatin, simvastatin, atorvastatin, pitavastatin, or rosuvastatin.

42-44. (cancelled)

45. (new) The method of Claim 22, wherein the therapy/treatment results in a decrease in serum levels of cholesterol, low-density lipoproteins, very low-density lipoproteins, triglycerides and/or apolipoprotein B; and/or an increase in serum levels of high-density lipoproteins and/or apolipoprotein A-I.

46. (new) The combination product of Claim 27, wherein the thrombin inhibitor or derivative is of the formula:

$$R^1O_2C\text{-}CH_2\text{-}(R)Cgl\text{-}(S)Aze\text{-}Pab\text{-}OH,$$

wherein R^1 represents linear or branched $C_{1\text{-}6}$ alkyl and the OH group replaces one of the amidino hydrogens in Pab, and the other therapeutic agent is a statin.

47. (new) The combination product of Claim 27, wherein the thrombin inhibitor or derivative is of the formula:

R^1O_2C-CH_2-(*R*)Cgl-(*S*)Aze-Pab-OH,

wherein R^1 represents linear or branched C_{1-6} alkyl and the OH group replaces one of the amidino hydrogens in Pab, and the other therapeutic agent is lovastatin, pravastatin, fluvastatin, simvastatin, atorvastatin, pitavastatin, or rosuvastatin.

48. (new) The combination product of Claim 27, wherein the thrombin inhibitor or derivative is of the formula:

EtO_2C-CH_2-(*R*)Cgl-(*S*)Aze-Pab-OH,

wherein Et represents ethyl and the OH group replaces one of the amidino hydrogens in Pab, and the other therapeutic agent is a statin

49. (new) The combination product of Claim 27, wherein the thrombin inhibitor or derivative is of the formula:

EtO_2C-CH_2-(*R*)Cgl-(*S*)Aze-Pab-OH,

wherein Et represents ethyl and the OH group replaces one of the amidino hydrogens in Pab, and the other therapeutic agent is lovastatin, pravastatin, fluvastatin, simvastatin, atorvastatin, pitavastatin, or rosuvastatin.

50. (new) The combination product of Claim 27, wherein the thrombin inhibitor or derivative is:

Ph(3-Cl)(5-$OCHF_2$)-(*R*)CH(OH)C(O)-(*S*)Aze-Pab;

Ph(3-Cl)(5-$OCHF_2$)-(*R*)CH(OH)C(O)-(*S*)Aze-Pab(2,6-diF); or

Ph(3-Cl)(5-OCH_2CH_2F)-(*R*)CH(OH)C(O)-(*S*)Aze-Pab,

and the other therapeutic agent is a statin.

51. (new) The combination product of Claim 27, wherein the thrombin inhibitor or derivative is:

Ph(3-Cl)(5-$OCHF_2$)-(*R*)CH(OH)C(O)-(*S*)Aze-Pab(OMe);

Ph(3-Cl)(5-$OCHF_2$)-(*R*)CH(OH)C(O)-(*S*)Aze-Pab(2,6-diF)(OMe); or

Ph(3-Cl)(5-OCH_2CH_2F)-(*R*)CH(OH)C(O)-(*S*)Aze-Pab(OMe),

and the other therapeutic agent is a statin.

52. (new) The combination product of Claim 27, wherein the thrombin inhibitor or derivative is:

Ph(3-Cl)(5-$OCHF_2$)-(*R*)CH(OH)C(O)-(*S*)Aze-Pab;

Ph(3-Cl)(5-$OCHF_2$)-(*R*)CH(OH)C(O)-(*S*)Aze-Pab(2,6-diF); or

Ph(3-Cl)(5-OCH_2CH_2F)-(*R*)CH(OH)C(O)-(*S*)Aze-Pab,

and the other therapeutic agent is lovastatin, pravastatin, fluvastatin, simvastatin, atorvastatin, pitavastatin, or rosuvastatin.

53. (new) The combination product of Claim 27, wherein the thrombin inhibitor or derivative is:

Ph(3-Cl)(5-$OCHF_2$)-(*R*)CH(OH)C(O)-(*S*)Aze-Pab(OMe);

Ph(3-Cl)(5-$OCHF_2$)-(*R*)CH(OH)C(O)-(*S*)Aze-Pab(2,6-diF)(OMe); or

Ph(3-Cl)(5-OCH_2CH_2F)-(*R*)CH(OH)C(O)-(*S*)Aze-Pab(OMe),

and the other therapeutic agent is lovastatin, pravastatin, fluvastatin, simvastatin, atorvastatin, pitavastatin, or rosuvastatin.